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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,117	07/31/2003	Hilda Elizabeth Smith	2183-6055US	5350

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EXAMINER	
HINES, JANA A	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/632,117	SMITH, HILDA ELIZABETH	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/20/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of claims 11-15 in the reply filed on August 4, 2004 is acknowledged. Claims 1-10 and 16-20 have been withdrawn from consideration. Claim 11-15 are pending in this office action.

Specification

3. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 11 is drawn to an isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof.

The instant specification and claims are encompassing currently unidentified nucleic acid molecules and claiming that these nucleic acids have the capability of hybridizing to SEQ ID NO: 8-45 or fragments thereof. Therefore, there is evidence that claimed nucleic acids have not yet been identified. Moreover, the instant specification fails to disclose the specific nucleic acid molecules; rather the specification broadly defines the sequences to be any nucleic acid molecule of a *Streptococcus* origin, including one or two nucleic acids without any discretion. In view of the lack of evidence, it is apparent that Applicants were not in possession of all or many nucleic acid molecules that hybridize to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof at the time of filing the instant application.

The specification and claims lack sufficient written description of the generically claimed isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence. The specification does not place any structure, chemical or absolute functional limitations on the nucleic acid molecule per se. It is noted that the nucleic acid molecule only be capable of hybridizing and not that the molecule actually hybridizes to any of SEQ ID NO:8-45. The recitation of a nucleic acid molecule does not convey a common structure or function. The scope of the claims includes numerous structural variants and the genus is highly variant because a significant number of structural differences between the genus members are permitted. The specification fails to provide guidance

on the structure of the nucleic acid molecules. Structural features that could distinguish molecules in the genus from others in the class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed.

The skilled artisan cannot envision the detailed structure of an isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

The nucleic acid molecule comprising one or more nucleic acids is defined by its activity of function, i.e., the capability to hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof. While the description of the ability of the claimed nucleic acid molecule which hybridizes may generically describe the nucleic acid molecule's function, it does not describe the nucleic acid molecule itself. The hybridization capability distinction is a purely functional distinction. Thus, a description of the nucleic acid molecule by what it does, such as hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof is insufficient. Since the disclosure fails to describe the common attributes or structural characteristics that identify the members of the genus, and because the genus of nucleic acid molecules of Streptococcus origin is highly variable, the function of hybridization alone is insufficient to describe the genus of nucleic acid molecules.

An adequate description requires more than a mere statement that it is part of the invention. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Encoding distinguishes the claimed nucleotide sequences from unclaimed sequences only by what they do, which is a purely functional distinction. Even where there is an actual reduction to practice, which may demonstrate possession of an embodiment of an invention, it does not necessarily describe what the claimed invention is. The instant claims describe a nucleic acid molecule described by its function i.e., hybridization, however this description does not describe the claimed nucleic acid molecules themselves. See also, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), where the court held that a generic statement that defines a genus of nucleic acids by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". Thus, in the absence of an isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof adequately described, an isolated or recombinant nucleic acid molecules described only by its ability to hybridize fails to meet the written description requirements.

The written description in this case only sets forth specific sequences, therefore the written description is not commensurate in scope with the claims drawn to fragments thereof. Neither the specification nor the claims teach how to define fragments thereof. Neither the claims nor the specification teach how to obtain such fragments. There is no guidance as to what the fragments are; or what fragments can or cannot be used in the nucleic acid molecule being claimed. The specification does not include structural examples fragments thereof. Thus, the resulting r fragment could result in a complex not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically named sequences, the skilled artisan cannot envision the detailed structure of the fragments thereof, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. Furthermore, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed

by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus.

Claim 15 is drawn to a vaccine comprising the isolated or recombinant nucleic acid molecule of claim 11. The written description in this case fails to set forth a vaccine comprised of a nucleic acid molecule, therefore the written description is not commensurate in scope with the claim drawn to a vaccine. The specification fails to provide a description drawn to a vaccine comprised of a nucleic acid molecule that consist of one or two nucleic acids. Neither the claims nor the specification teach how to use these nucleic acids in an effective vaccine. There is no guidance as to what nucleic acids are capable of hybridizing to SEQ ID NO:8-45 and be used within the vaccine being claimed. The specification does not include structural examples of a vaccine comprising the isolated or recombinant nucleic acid molecule of claim 11. Thus, the resulting composition could result in vaccines not taught and enabled by the specification. However, there is no support within the specification that the naked nucleic acids of the instant claims will function at all. There is no evidence that antibody production was elicited. Furthermore, there is no description as to what the additional components are necessary to create a vaccine. Therefore the effects of these changes are largely unpredictable and likewise present an unreliable correspondence between the claimed polynucleotide and the art recited vaccination procedures.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

One skilled in the art would reasonably conclude that the disclosure fails to provide a representative number of species when the claims provide no structure to the described claimed genus. Applicants were not in possession of the claimed genus because the specification does not convey to one of skill in the art a representative number of nucleic acid molecules as described by their structure and function. As such, generic sequences or nucleic acids that are unrelated via structure and function are highly variant and failed to convey by way of written description possession at the time of filling. Thus the specification lacks written description for the claimed invention and full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph. Moreover, one skilled in the art would not recognize that applicants had possession of the claimed isolated or recombinant nucleic acid molecules.

5. Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to an isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof. The specification fails to identify an

isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof with the recited characteristics. There is no teaching of how to determine which nucleic acids should comprise the nucleic acid molecule. Therefore, the specification fails to enable an isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof. The specification is not enabled for an isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof because the specification fails to teach the identity of such sequences.

The specification lacks any written description of a structure or relevant identifying characteristics of a representative number of nucleic acids sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. The specification fails to teach what the critical nucleic acid which can or cannot be or what nucleic acids can be inserted, deleted or substituted to be capable of hybridization. The art teaches that replacement of a single nucleic acid residue may lead to both structural and functional changes in the biological activity of a protein. One of skill in the art would be reduced to merely randomly altering nucleic acids which would lead to unpredictable results regarding the isolated or recombinant nucleic acid molecule. The art is replete with examples of one nucleotide being deleted or inserted at a single place within the coding sequence and thus being frame shifted.

Several publications document the unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Gerhold et al. [BioEssays, Volume 18, Number 12, pages 973-981 (1996)]; Wells et al. [Journal of Leukocyte biology, Volume 61, Number 5, pages 545-550 (1997)]; and Attwood, [Science, 290:471-473, (29 October 2000)].

In absence of further guidance, the skilled artisan would have to discover what the appropriate nucleic acids would be. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. Such need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use of an isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof. The inclusion of any nucleic acid in any location within the molecule would not predictably result in the isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof. The specification does not provide guidance on how any nucleic acids can be used to produce a stable nucleic acid molecule. No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict which combination of nucleic acids would result in the desired nucleic acid molecule.

Accordingly, one of skill in the art would be required to perform undue experimentation to use any nucleic acid at any location to produce such a nucleic acid molecule. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation.

Claim 15 is drawn to a vaccine comprising the isolated or recombinant nucleic acid molecule of an isolated or recombinant nucleic acid molecule of a *Streptococcus* origin comprising a nucleotide sequence capable of hybridizing to a nucleotide sequence selected from the group of nucleotide sequence consisting of any one of SEQ ID NO:8-45 or fragments thereof.

The specification is not enabled for using the nucleic acid molecules as vaccines for the following reasons. There is absolutely no demonstration of protective immunity upon administration in any animal model of disease. The instant specification fails to provide any experiments that show that such vaccines would be effective in protecting a human or other animal against a Streptococcal or any other bacterial infection. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to an infection or disease induction. The vaccine art is highly unpredictable and the instant specification fails to provide any information that the recited vaccine would provide any immunity to any type of patient against any type of infection. There are no immunological experiments provided to demonstrate that the claimed vaccine is capable of mounting an effective immune response. More importantly, there are no challenge experiments to demonstrate that an animal immunized with the nucleic acid molecule that would be protected from an infection.

There are no protocols provided which demonstrate that the nucleic acid molecule would be effective in immunization, nor are their protocols detailing the amount of nucleic acid molecule needed to mount a sufficient immune response. There is no teaching as to what the most effective route of administration for the claimed vaccines. It is well known that nucleic acids are not effective in all routes of administration, since the nucleic acids are known to degrade. There is merely a general outline of vaccines that do not apply directly to the instantly claimed invention. Janeway et al., *Immunobiology: The Immune System in Health and Disease* (1997) teach that it is not clear how DNA vaccination actually works, i.e., do muscle cells elicit the immune response or do tissue dendritic cells take up the DNA and express it? Furthermore, the art is not clear on whether or how lymphocytes encounter the antigen if it is expressed in muscle cells. Finally, Janeway states that it is unknown how safe the approach is and how generally applicable nucleic acid vaccination will be. The art teaches administration of the DNA as being coated onto minute metal particles that penetrate the skin and enter into the muscle beneath. See page 13:33. The art teaches that it is unclear whether antibodies are even produced, yet the instant claims imply antibody production that will elicit a protective response. It is well known in the art that adjuvants stimulate the immune response to the antigen with which it is mixed, however the vaccine does not include adjuvants. The specification teaches the inclusion of an adjuvant to the vaccine, thus it appears that an adjuvant would be necessary in a vaccine capable of establishing resistance to an infection. See Janeway-Travers. *Immunobiology: The immune system in health and disease.* Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy. The claims and specification fail to disclose the type of vaccine that should be administered. The claims fail to recite subjects for which

the vaccine can be administered, dosage schemes, administration modes and the like. Therefore the specification fails to provide support for the claims. It is well known that merely generating an immune response does not equate to providing protective immunity.

This demonstration is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of preventing any infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced. The specification fails to teach the identity a vaccine with the claimed ability. Furthermore, the specification fails to adequately disclose a description of the claimed vaccines, thus a skilled artisan would be required to de novo locate, identify and characterize the claimed vaccines with the recited abilities. Accordingly, this would require undue experimentation given the fact that the specification is completely lacking in teachings as to vaccines with the broadly claimed protection abilities. Thus, the art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy. In the absence of a teaching of the claimed isolated or recombinant nucleic acid molecules, the specification is not enabled for vaccines as claimed. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to use the invention as claimed.

Prior Art

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Smith et al., (US Patent 5,610,011) teach virulence a nucleic acid molecule of a *Streptococcus suis* origin capable of hybridizing to any one of SEQ ID

NO:8-45. US Patent 5,610,011 further teach vectors, host cells and vaccines containing polynucleotides. Smith et al., (1992) teach an isolated or recombinant nucleic acid molecule of a *Streptococcus* origin capable of hybridizing to any one of SEQ ID NO: 8-45, host cells and vectors.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines

October 26, 2004

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